REMARKS

Claims 1 and 3-6 are under examination, and claims 7-21 have been withdrawn. Applicants respectfully request that the amendment to claim 1 be entered as it places the claims in better condition for allowance. This amendment is fully supported in the application as filed by, for example, pages 23-27.

Applicants acknowledge with appreciation the withdrawal of the previous rejection under 35 U.S.C. §102(e). The claims currently stand rejected under 35 U.S.C. §112, first paragraph, and under 35 U.S.C. §103(a). Reconsideration of the application is respectfully requested.

Rejections under 35 U.S.C. §112, First Paragraph

Claims 1-6 are rejected under 35 U.S.C. §112, first paragraph, because the specification, although enabling for *in vitro* methods, is allegedly not enabling for a method of activating the immune system in a mammal. The Examiner asserts that the specification does reasonably provide enablement for a method of activating the immune system in a mammal in need thereof, wherein the mammal has a condition selected from the group consisting of viral infection, bacterial infection, fungal infection, cancer, and graft v. host disorders, comprising administering to the mammal an effective amount of an IMXP-888 polypeptide, wherein the IMXP-888 polypeptide is encoded by a sequence that is at least 80% homologous to a polynucleotide sequence that encodes residues 18 to 375 of SEQ ID NO:3. The Examiner further states that the "structural and functional characteristics of said peptides are not defined in the claim." (Office Action at 4.) Applicants submit that this rejection is been mooted by amendment.

The currently presented claims recite both structural and functional limitations on the IMXP-888 polypeptides for use in the claimed methods. Applicants are claiming only the use of IMXP-888 polypeptides which are structurally conserved (*i.e.*, encoded by a sequence that is at least 80% homologous to a polynucleotide sequence that encodes residues 18 to 375 of SEQ ID NO:3), and which are functional in an *in vitro* assay. In particular, the claims now recite that the IMXP-888 for use in the claimed methods "induces cytokine production or calcium mobilization in natural killer cells, peripheral blood monocytes, or monocytes when tested in an *in vitro* assay." As previously noted by the Examiner, Applicants have demonstrated through the use of *in vitro* assays particular, previously unknown functions for the IMXP-888 proteins. The discovery of these previously unknown functions using a

battery of *in vitro* tests supports the enablement of the claimed methods of the invention. Further, there is no evidence of record that these *in vitro* functions do not correlate to clinical applications. In fact, the evidence of record supports the correspondence of *in vitro* tests to *in vivo* applications.

For example, in Feldman et al. (a reference that was cited by the Office) the author states that his experiments *in vitro* and *in vivo* with rheumatoid synovium led them to propose inhibiting TNF-alpha would be clinically useful (*see* second paragraph). Thus, according to Feldman et al., the results of *in vitro* experiments actually supports clinical applications. Accordingly, the evidence of record supports the enablement of the currently claimed invention.

Accordingly, reconsideration and withdrawal of the rejection for lack of enablement is requested.

Claims 1and 3-6 are also rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. (Office Action at 6.) The Examiner asserts that the specification fails to define all polypeptides that are at least 80% homologous to a polypeptide sequence that encodes residues 18 to 375 of SEQ ID NO:3 that can be used in a method of activating the immune system in a mammal. Citing *Fiers v. Revel*, the Examiner states that "Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required." (Office Action at 7.) The Examiner also cites *Vas-Cath Inc. v. Mahurkar*, and *University of California v. Eli Lilly and Co.* in support of the rejection.

Applicants' claimed invention relates to the new use of polypeptides; the claims are not to the polypeptides themselves. In addition, not only were IMXP-888 polypeptides known and described by others, the genes encoding human and murine IMXP-888 polypeptides were already cloned. In both *Lilly* and *Fiers v. Revel*, (1) the claims were directed to polynucleotides in and of themselves, and (2) the claims that were found invalid for lack of written description were so because the genes had never been cloned. Here the claims are directed to methods of using proteins, and the genes encoding those proteins had been cloned and are known. Therefore, Applicants submit that the instant factual situation is distinct from both *Lilly* and *Fiers v. Revel*, and the holdings in those cases are inapplicable here. Instead, as in *Vas-Cath*, one of skill in the art reviewing Applicants' specification would

know that Applicants' had identified a new function for IMXP-888, and were in possession of the claimed invention.

Here, the specification describes several examples of IMXP-888 polypeptides within the recited scope (*e.g.*, human and murine soluble fragments, *inter alia*), and describes how to generate and test additional IMXP-888 polypeptides. The Examiner has not disputed that generation of variants of these polypeptides is described, and that testing them for function is also described, and that both are readily accomplished by those skilled in the art. Further, the Examiner has not addressed Applicants' reference in the previous response to the USPTO's "Synopsis of Application of Written Description Guidelines", Example 14, pages 53-55. The claim of Example 14 recites a protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A->B. The disclosure of Example 14 provides a single species (SEQ ID NO:3) that has actually been reduced to practice, and describes an assay for identifying the variants having the desired catalytic activity. In the instant case, these guidelines issued by the Office indicate that the currently claimed invention is fully supported by the written description of the instant application.

In view of the above, Applicants respectfully request that the rejections under 35 USC § 112, first paragraph, be reconsidered and withdrawn.

Rejections under 35 U.S.C. §103(a)

Claims 1 and 3-6 are rejected under 35 U.S.C. §103(a) in view of any one of US Patent Publication 2002/0197674, WO 01/70977, or WO 01/00673, in view of US Patent No. 5,807,862. The Examiner asserts that Applicant has argued the references individually and not their combination. (Office Action at 8.) The '862 patent is cited for teaching the treatment of viral infection by stimulating the immune system in response to FGF administration. (Office Action at 9.) The Examiner states that because viral infection can be treated by activating the immune system as taught by the '862 patent, one would be motivated to use the method of administering IMXP-888 taught by 2002/0197674, WO 01/70977, or WO 01/00673 to activate the immune system in a mammal, wherein the mammal has a viral infection.

Applicants respectfully traverse. In the last Office Action, Applicants elaborated on why there was no motivation to combine the '862 patent with any of the other references. Specifically, the '862 patent related to inhibiting FGF. IMXP-888 is unrelated to FGF. IMXP-888s have some homology to the FGF- **Receptor** (the cognate for FGF), but there is no

evidence that IMXP-888 has any functional similarity with even the FGF-Receptor. There is certainly no evidence that it shares either functional or structural homology with the FGF disclosed in the '862 patent. Accordingly, there is no reason to combine the '862 patent, which deals entirely with unrelated compounds, with the references cited that disclose IMXP-888. However, the Examiner has not rebutted Applicants' remarks regarding this lack of motivation.

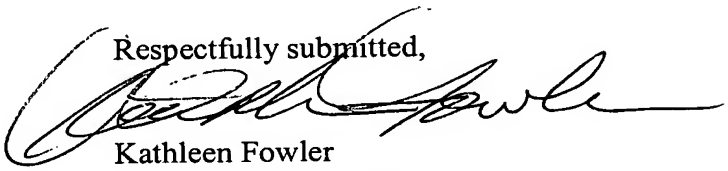
Further, even if any of these combinations of references is taken together, they do not suggest that IMXP-888 can be used in a method of activating the immune system in a mammal in need thereof, wherein the mammal has a viral infection. As noted previously, the art as a whole taught away from the presently claimed invention. However, the Examiner has not addressed or acknowledged Applicants' remarks regarding these teachings away. In addition, none of the references, alone or in combination, suggest using IMXP-888 with the recited structural and functional limitations in the claimed methods.

In conclusion, Applicants request that the rejection under 35 U.S.C. §103(a) be reconsidered and withdrawn.

CONCLUSION

Applicants submit that the presented claims are in condition for allowance. A favorable action is earnestly requested. Applicants' attorney invites the Examiner to call her at the number below if any issue remains outstanding.

Respectfully submitted,



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